erately severe rheumatoid arthritis, though they had little effect when the disease was severe (A. M. Marmont et al., in International Symposium on Non-Steroidal Anti-Inflammatory Drugs, Amsterdam, Excerpta Medica Foundation, 1965, p. 363). In ankylosing spondylitis, indomethacin has appeared to relieve pain more consistently than in other types of arthritis (F. D. Hart and P. L. Boardman, Brit. Med. J., 2:965, 1963). How it compares with aspirin and phenylbutazone in the treatment of spondylitis is not yet known.

Indomethacin has been used in combination with prednisone in a number of studies on patients with rheumatoid arthritis. The use of indomethacin permitted reduction of dosage of the steroid with all the patients in some studies, with fewer than half in others. The side effects of corticosteroids are much more serious than those thus far observed with indomethacin, and the combination, with reduced dosage of steroids, is well worth a trial where steroids cannot be eliminated altogether. It is not yet known whether indomethacin can be safely and effectively used in combination with such other anti-rheumatic drugs as phenylbutazone, gold salts and chloroquine.

Gouty arthritis.—In the treatment of acute gouty arthritis with indomethacin, many patients have shown improvement within about 48 hours (P. L. Boardman and F. D. Hart, Practitioner, 194:560, April, 1965). How the drug compares in effectiveness with colchicine and phenylbutazone can be determined only by better-controlled trials than those so far reported. The usefulness of indomethacin combined with a uricosuric agent such as probenecid (Benemid—Merck) in the treatment of chronic gouty arthritis is being investigated.

Osteoarthritis and other conditions.—In uncontrolled trials, indomethacin has been reported to be effective in relieving pain in osteoarthritis. A valid judgment of its usefulness must await further trials. It is not recommended by the manufacturer for such acute musculoskeletal disorders as bursitis, tendinitis, and synovitis.

Adverse effects.—Adverse effects, often severe, and requiring discontinuance of the drug in many patients, are common, and a few fatalities have been attributed to indomethacin. Among the most frequent adverse effects are headache, dizziness, gastrointestinal disturbances (nausea, anorexia, vomiting, diarrhea, bleeding and ulceration), and psychic disturbances. Whether significant hematologic, renal hepatic, or neurologic reactions occur is not clear. A fuller assessment of adverse effects will be possible only after longer use; indomethacin appears to be too hazardous to be substituted for aspirin when that drug is effective, but it may prove less hazardous than other anti-arthritic drugs.

Precautions and contraindications.—The manufacturer warns that indomethacin is contraindicated in patients with active peptic ulcer, gastritis, ulcerative colitis, and regional ileitis. Whether it crosses the placental barrier is not yet known, nor are its effects on the human fetus; therefore, indomethacin should not be used in pregnant women. The manufacturer also warns that there has been insufficient experience to warrant its use in children. Because of the frequency of dizziness, lightheadedness, and feelings of detachment, patients on indomethacin should be cautioned against operating motor vehicles or other machinery, climbing ladders, etc., and the drug should be used with great caution in patients with psychological difficulties, epilepsy or parkinsonism, since it sometimes aggravates these conditions.

Dosage and administration.—The recommended initial dose is 25 mg twice daily, with gradual increase as needed. Good response is often obtained with 100 mg daily, divided into four doses. Further improvement rarely occurs when the dose is increased above 150 or 200 mg a day. The drug should be given with food to reduce gastric irritation.

Conclusion.—Early clinical trials indicate that indomethacin is a useful addition to the group of drugs available for the treatment of rheumatoid arthritis and ankylosing spondylitis. Its place in the management of acute gouty arthritis and osteoarthritis is less clear; properly controlled trials are needed.

In the treatment of rheumatoid arthritis, aspirin is still the drug of first choice (see The Medical Letter, Vol. 7, p. 75, 1965, for a discussion of the side effects of aspirin). When effective doses of aspirin are not well tolerated, indomethacin may be used with lower doses of aspirin or, if necessary, substituted for it, before resort is had to corticosteroids. In patients already on corticosteroids, reduction of the steroid dosage and a decrease in steroid side effects can often be achieved by the addition of indomethacin.

If gastric ulceration occurs with either aspirin, phenylbutazone, or corticosteroids, indomethacin cannot be considered a safe substitute since it, too, causes gastric ulceration. In such cases, gold salts or chloroquine can be tried; these also have serious side effects, but they do not cause gastric ulceration.